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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/766,651	01/27/2004	Ronald A. Beyerinck	0003.0577/PC23195B	4574

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EXAMINER	
SASAN, ARADHANA	
ART UNIT	PAPER NUMBER
1615	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/766,651	BEYERINCK ET AL.	
	Examiner	Art Unit	
	ARADHANA SASAN	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 February 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22,24-26,30 and 39-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22, 24-26, 30 and 39-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The remarks, amendments, and Request for Continued Examination filed on 01/28/10 and the remarks and amendments filed on 02/19/10 are acknowledged.

2. Claims 1-21, 23, 27-29 and 31-38 were cancelled. Claim 22 was amended.

3. Claims 22, 24-26, 30 and 39-43 are included in the prosecution.

Continued Examination under 37 CFR 1.114

4. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 01/28/10 has been entered.

Response to Arguments

Rejection of claims under 35 USC § 102(a) and 102(e)

5. Applicant's arguments, see Page 5, filed 02/19/10, with respect to the rejection of claims 22-26, 30, 34-37 and 39-43 under 35 USC § 102(a) and under 35 USC § 102(e) as being anticipated by Babcock et al. (US 2001/0053791 A1) have been fully considered and are found persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, new ground(s) of rejection are made under 35 USC § 103(a).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 22, 24-26, 30 and 39-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Babcock et al. (US 2001/0053791 A1).

The claimed invention is a composition comprising a plurality of solid amorphous dispersion particles comprising a substantially amorphous drug and a polymer selected from the group consisting of hydroxypropyl methyl cellulose acetate succinate (HPMCAS), hydroxypropyl methyl cellulose phthalate (HPMC phthalate), cellulose acetate phthalate, cellulose acetate trimellitate, polyvinyl alcohols that have at least a portion of their repeat units in hydrolyzed form, polyvinyl pyrrolidone, poloxamers, and blends thereof wherein the particles have an average diameter of at least 40 μm and a bulk specific volume of less than 5 mL/g, and wherein at least 90 vol % of said particles have diameters of greater than 10 μm and wherein the particles are formed by a spray drying process, the process comprising the steps (a) forming a feed solution comprising the drug, the polymer, and a solvent in which both the drug and the polymer are soluble; (b) directing the feed solution to a spray-drying apparatus; (c) atomizing the feed solution into droplets in the spray-drying apparatus; and (d) contacting the droplets with a drying gas to form the particles.

Babcock teaches spray drying as a process that breaks up liquid mixtures into small droplets (atomization) and rapidly removing solvent from the mixtures in a vessel such as a spray-drying apparatus where there is a strong driving force for evaporation of solvent from the droplets (Page 6, [0063]). "In the case of spray-drying, the droplets generally dry prior to impinging on a surface, thus forming particles of solid amorphous dispersion on the order of 1 to 200 micrometers in diameter … For example, a solution of drug and a dispersion polymer such as HPMCAS in acetone may be suitably spray-dried by spraying the solution at a temperature of 50.degree. C. (the vapor pressure of acetone at 50º C is about 0.8 atm) into a chamber held at 0.01 to 0.2 atm total pressure by connecting the outlet to a vacuum pump. Alternatively, such a solution may be sprayed into a chamber where it is mixed with nitrogen gas at a temperature of 80ºC to 250ºC and pressure of 1.0 to 1.2 atm" (Pages 6-7, [0063]).

Babcock does not expressly teach at least 90 vol % of the particles have diameters of greater than 10 μm.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare an amorphous solid dispersion by mixing an amorphous drug with a polymer (such as HPMCAS) and spray drying the resulting solution in order to produce particles in a range from 1 to 200 μm, modify the process parameters during the process of routine experimentation in order to achieve the desired particle size, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because modifying the particle size of a spray dried composition is considered part of routine

optimization and the recited limitation of at least 90 vol % of the particles having diameters of greater than 10 μm would have been obvious variants unless there is evidence of criticality or unexpected results.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Regarding instant claim 22, the limitation of a composition comprising a plurality of solid amorphous dispersion particles comprising a substantially amorphous drug and a polymer selected from the group consisting of hydroxypropyl methyl cellulose acetate succinate, hydroxypropyl methyl cellulose phthalate, cellulose acetate phthalate, cellulose acetate trimellitate, polyvinyl alcohols that have at least a portion of their repeat units in hydrolyzed form, polyvinyl pyrrolidone, poloxamers, and blends thereof is obvious over the particles of solid amorphous dispersion comprising a drug and a dispersion polymer such as HPMCAS, as taught by Babcock (Pages 6-7, [0063]). The limitation of the particles having an average diameter of at least 40 μm and the limitation of at least 80 vol % of the particles having diameters of greater than 10 μm are obvious over the particles that are on the order of 1 to 200 micrometers in diameter, as taught by Babcock (Pages 6-7, [0063]). The limitation a bulk specific volume of less than 5 mL/g is a property of the particles that is inseparable from the particles. Babcock teaches the components of the composition (the drug, the polymer, and the solvent), the particle

size (1-200μm), and the process by which the particles are prepared (preparing a solution of the drug and polymer in the solvent, spray-drying the solution). Therefore, the bulk specific volume (which is calculated by dividing a known volume of particles by the weight of the particles) is obvious over the teaching of Babcock, absent any evidence of criticality. The limitations of the spray drying process are obvious over the spray drying process taught by Babcock (Pages 6-7, [0063]). The limitation of at least 90 vol % of the particles having diameters of greater than 10μm is obvious over the particles that are on the order of 1 to 200 micrometers in diameter, as taught by Babcock (Pages 6-7, [0063]).

Regarding instant claim 24, the limitation of the particles having an average diameter of at least 50μm is obvious over the particles that are on the order of 1 to 200 micrometers in diameter, as taught by Babcock (Pages 6-7, [0063]).

Regarding instant claim 25, the limitation of a bulk specific volume of less than 4 mL/g is a property of the particles that is inseparable from the particles. Babcock teaches the components of the composition (the drug, the polymer, and the solvent), the particle size (1-200μm), and the process by which the particles are prepared (preparing a solution of the drug and polymer in the solvent, spray-drying the solution) (Pages 6-7, [0062] – [0063] and Page 9, [0086]). Therefore, the bulk specific volume (which is calculated by dividing a known volume of particles by the weight of the particles) is obvious over the teaching of Babcock, absent any evidence of criticality.

Regarding instant claim 26, the limitation of the drug is obvious over the glycogen phosphorylase inhibitor taught by Babcock (Page 1, [0001] – [0002]).

Regarding instant claim 30, the limitation of the hydroxypropyl methyl cellulose acetate succinate is obvious over the hydroxypropyl methyl cellulose acetate succinate (HPMCAS) taught by Babcock (Page 5, [0050] and Pages 6-7, [0063]).

Regarding instant claims 39-41, the limitations of the average droplet diameter, D_{10} and D_{90} are obvious over the droplet size of 1-200μm, as taught by Babcock (Pages 6-7, [0063]). Babcock teaches the components of the composition (the drug, the polymer, and the solvent), the particle size (1-200μm), and the process by which the particles are prepared (preparing a solution of the drug and polymer in the solvent, spray-drying the solution). The average droplet diameter, $D_{10,}$ and D_{90} are properties that are inseparable from the droplets taught by Babcock, absent any evidence of criticality. "Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. (MPEP 2112.01).

Regarding instant claims 42-43, the limitations of the span of the droplets are obvious over the droplet size of 1-200μm, as taught by Babcock (Pages 6-7, [0063]). Babcock teaches the components of the composition (the drug, the polymer, and the solvent), the particle size (1-200μm), and the process by which the particles are prepared (preparing a solution of the drug and polymer in the solvent, spray-drying the solution). The span of the droplets is a property that is inseparable from the droplets taught by Babcock, absent any evidence of criticality. "Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and

its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. (MPEP 2112.01).

8. Claims 22, 24-25, 30 and 39-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Albano et al. (US 6,350,786 B1).

Albano teaches a stable complex composed of a water-insoluble polymer carrier and a therapeutically active compound in stable amorphous form (Col. 3, lines 45-50). The polymers include cellulose acetate phthalate, hydroxypropyl methyl cellulose phthalate, and hydroxypropyl methyl cellulose acetate succinate (Col. 6, lines 43-55). The therapeutically active compound and the ionic polymer are dissolved in a common solvent (such as ethanol, methanol, acetone, etc.), and by means of spray drying, the solvent is evaporated, leaving the active compound microprecipitated in amorphous form in the polymer matrix (Col. 7, lines 40-49). Albano exemplifies spray drying a solution of an active compound (Compound III) and a polymer (such as hydroxypropylmethylcellulose phthalate) (Col. 10, lines 35-42). Albano teaches that the desired mean particle size is 90% particles in the 50-400 μm range (Col. 10, lines 30-31).

Albano does not expressly teach at least 90 vol % of the particles have diameters of greater than 10 μm.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare a complex composed of a water-insoluble polymer carrier and a therapeutically active compound in stable amorphous form by spray

drying, as suggested by Albano, modify the process parameters during the process of optimizing spray drying in order to achieve the desired particle size, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because modifying the particle size of a spray dried composition is considered part of routine optimization and the recited limitation of at least 90 vol % of the particles having diameters of greater than 10 μm would have been obvious variants unless there is evidence of criticality or unexpected results. Moreover, Albano teaches that the desired mean particle size is 90% particles in the 50-400 μm range (Col. 10, lines 30-31).

Regarding instant claim 22, the limitation of a composition comprising a plurality of solid amorphous dispersion particles comprising a substantially amorphous drug and a polymer selected from the group consisting of HPMCAS, HPMC phthalate, cellulose acetate phthalate, cellulose acetate trimellitate, polyvinyl alcohols that have at least a portion of their repeat units in hydrolyzed form, polyvinyl pyrrolidone, poloxamers, and blends thereof is obvious over the complex composed of a water-insoluble polymer carrier such as cellulose acetate phthalate, hydroxypropyl methyl cellulose phthalate, and hydroxypropyl methyl cellulose acetate succinate (Col. 6, lines 43-55) and a therapeutically active compound in stable amorphous form (Col. 3, lines 45-50) as taught by Albano. The limitation of the particles having an average diameter of at least 40 μm and the limitation of at least 80 vol % of the particles having diameters of greater than 10 μm are obvious over the desired mean particle size of 90% particles in the 50-400 μm range, as taught by Albano (Col. 10, lines 30-31). The limitation a bulk specific

volume of less than 5 mL/g is a property of the particles that is inseparable from the particles. Albano teaches the components of the composition (the drug, the polymer, and the solvent), the particle size (50-400 μm), and the process by which the particles are prepared (preparing a solution of the drug and polymer in the solvent, spray-drying the solution). Therefore, the bulk specific volume (which is calculated by dividing a known volume of particles by the weight of the particles) is obvious over the teaching of Albano, absent any evidence of criticality. The limitations of the spray drying process are obvious over the spray drying process taught by Albano (Col. 10, lines 35-42). The limitation of at least 90 vol % of the particles having diameters of greater than 10μm is obvious over the mean particle size that is 90% particles in the 50-400 μm range, as taught by Albano (Col. 10, lines 30-31).

Regarding instant claim 24, the limitation of the particles having an average diameter of at least 50μm is obvious over the mean particle size that is 90% particles in the 50-400 μm range, as taught by Albano (Col. 10, lines 30-31).

Regarding instant claim 25, the limitation of a bulk specific volume of less than 4 mL/g is a property of the particles that is inseparable from the particles. Albano teaches the components of the composition (the drug, the polymer, and the solvent), the particle size (50-400 μm), and the process by which the particles are prepared (preparing a solution of the drug and polymer in the solvent, spray-drying the solution) (Col. 10, lines 35-42). Therefore, the bulk specific volume (which is calculated by dividing a known volume of particles by the weight of the particles) is obvious over the teaching of Albano, absent any evidence of criticality.

Regarding instant claim 30, the limitation of the hydroxypropyl methyl cellulose acetate succinate is obvious over the hydroxypropyl methyl cellulose acetate succinate (HPMCAS) taught by Albano (Col. 6, lines 43-55).

Regarding instant claims 39-41, the limitations of the average droplet diameter, D_{10} and D_{90} are obvious over the particle size (50-400 μm), and the process by which the particles are prepared (preparing a solution of the drug and polymer in the solvent, spray-drying the solution) as taught by Albano (Col. 10, lines 35-42). The average droplet diameter, $D_{10,}$ and D_{90} are properties that are inseparable from the droplets/particles taught by Albano, absent any evidence of criticality. "Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. (MPEP 2112.01).

Regarding instant claims 42-43, the limitations of the span of the droplets are obvious over the particle size (50-400 μm), and the process by which the particles are prepared (preparing a solution of the drug and polymer in the solvent, spray-drying the solution) as taught by Albano (Col. 10, lines 35-42). The span of the droplets is a property that is inseparable from the droplets/particles taught by Albano, absent any evidence of criticality. "Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. (MPEP 2112.01).

9. Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Albano et al. (US 6,350,786 B1) in view of Martin et al. (US 4,344,934).

Albano does not expressly teach a drug from the Markush group of claim 26.

Martin teaches spray drying a solution of griseofulvin (a known antifungal drug) and a polymer (Col. 4, lines 5-7 and Col. 8, lines 13- 16).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare a complex composed of a water-insoluble polymer carrier and a therapeutically active compound in stable amorphous form by spray drying, as suggested by Albano, modify the process parameters during the process of optimizing spray drying in order to achieve the desired particle size, use the antifungal drug that is spray dried with a polymer, as taught by Martin, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because the use of known technique to improve similar devices (methods, or products) in the same way is obvious. Please see MPEP 2141. In this case, Albano teaches the advantage of increases in bioavailability by producing a complex of an amorphous drug and a polymer (Col. 1, lines 11-17).

Regarding instant claim 26, the limitation of the drug would have been obvious over the amorphous drug taught by Albano (Col. 1, lines 11-17) and by the antifungal griseofulvin taught by Martin (Col. 4, lines 5-7 and Col. 8, lines 13- 16).

Conclusion

13. No claims are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax, can be reached at 571-272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Aradhana Sasan/
Examiner, Art Unit 1615

/Humera N. Sheikh/
Primary Examiner, Art Unit 1615